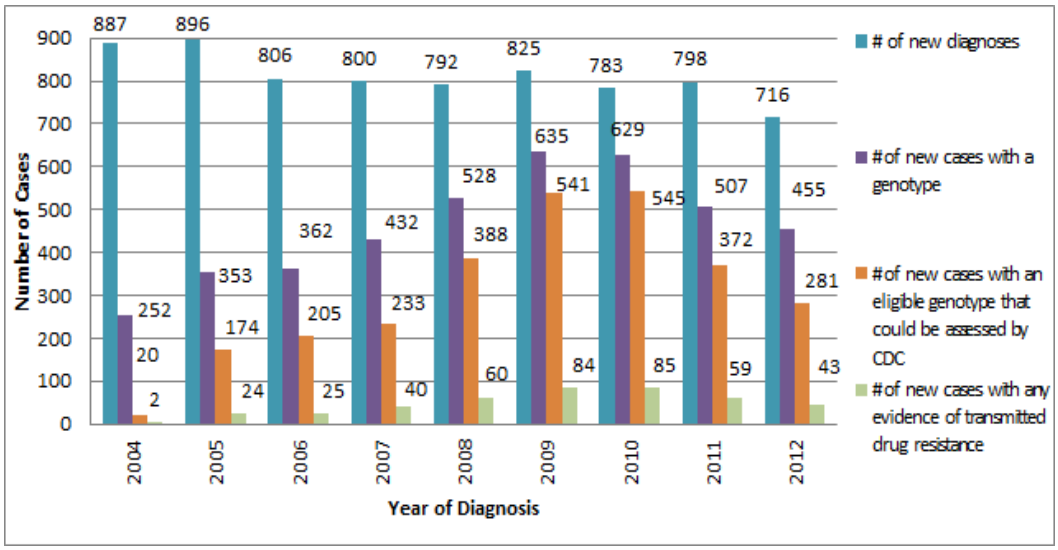
HIV Genotype Surveillance in Michigan 2004-2012

Introduction

The state of Michigan has collected baseline viral genotype sequence data on newly diagnosed HIV positive individuals since October of 2004. Prior to June of 2010 remnant diagnostic HIV serum specimens were collected statewide from sites such as hospitals, private physicians, community-based organizations, blood banks, and local health departments and sequenced free-of-charge for patients as part of a CDC-funded initiative called VARHS (Variant Atypical and Resistant HIV Surveillance). Additionally, private labs began submitting electronic sequences from samples collected during routine HIV care as early as 2006. In June 2010, CDC funding for genotyping under the VARHS protocol ended and since that time genetic surveillance has relied solely on genotypes run in the course of care by practitioners with test results reported to MDCH (MCL 333.5114). Figure 1 shows a completeness cascade of collected genotypes from 2004 through 2012. For each year the total number of new HIV cases diagnosed in Michigan and the fraction of those cases with a viral genotype collected by MDCH are presented. These are followed by the number of viral genotypes collected by MDCH that represent baseline sequences – defined as those run on newly diagnosed cases (<6 months) that are unlikely to already have initiated antiretroviral therapy. Finally, the number of new cases with evidence of drug resistance (TDRM) is presented. Of note is the decrease in the number of genotypes collected by MDCH after 2010 attributable to the loss of federal funding for VARHS.

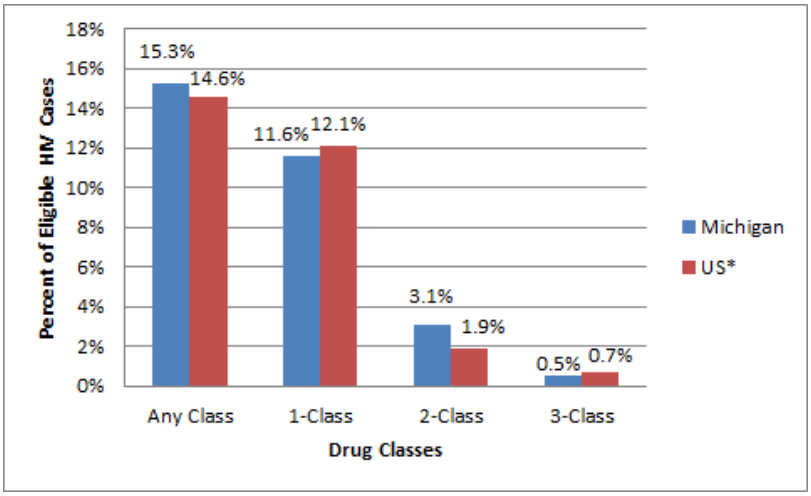
Figure 1: Genotype Completeness in Michigan, 2004-2012



Transmitted Drug-Resistant Mutation (TDRM)

In the period from 2004 through 2012, 15.3% (n=422) of new Michigan HIV cases with an eligible genotype collected by MDCH within 6 months of the patient's diagnosis date showed evidence of TDRM. Because these newly diagnosed individuals have yet to start treatment, the presence of any HIV drug resistance mutations in their HIV sequence indicates that the resistant virus was transmitted to them at the time of their infection. Michigan, a moderate

Figure 2: Percent of Eligible Cases with TDRM, by Number of Drug Classes, 2004-2012 (n = 2,759)



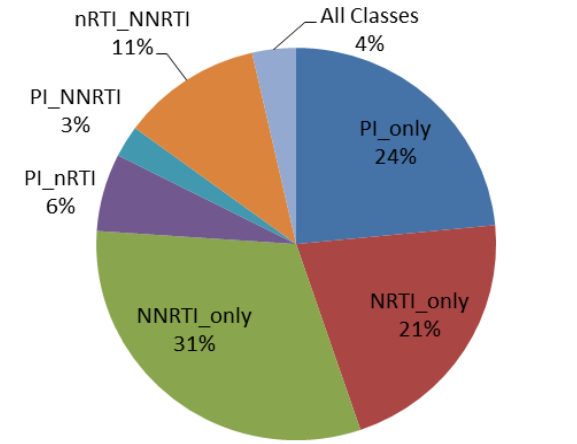
* National analysis only considered sequences within 3 month of diagnosis.

morbidity state of approximately 800 new HIV infections diagnosed annually, has rates of TDRM comparable to national rates for the three most common classes of anti-retroviral drugs – protease inhibitors (PI), nucleoside reverse transcriptase inhibitors (NRTI) and non-nucleoside reverse transcriptase inhibitors (NNRTI). PI's interfere with the protease enzyme that HIV uses to produce infectious viral particles. NRTI's and NNRTI's both interfere with the step in the HIV life cycle where the enzyme reverse transcriptase converts HIV RNA to HIV DNA. NRTI's are faulty DNA building blocks that when incorporated into the newly forming HIV DNA produce a faulty chain that cannot maintain its integrity. This essentially prevents HIV from being replicated within a cell. NNRTI's bind to reverse transcriptase enzymes interfering with it's ability to convert the HIV RNA to HIV DNA.

TDRM by Drug Class

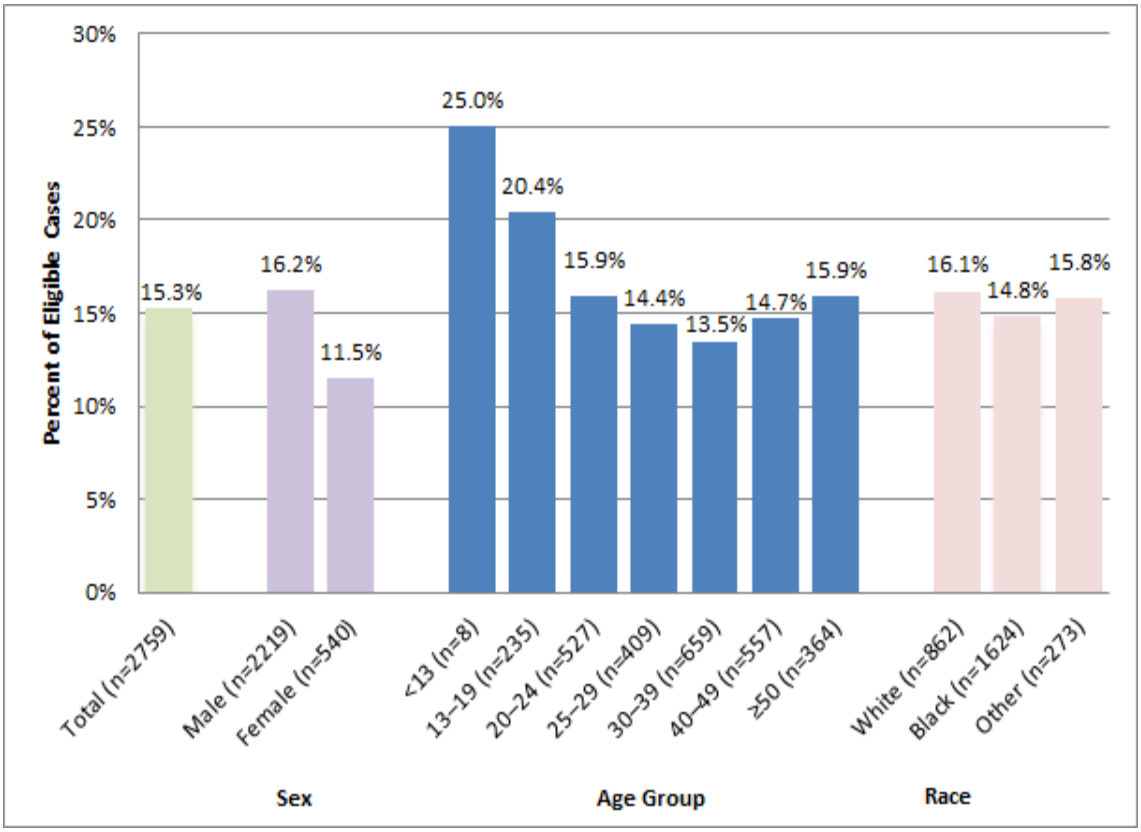
Of the 422 Michigan HIV cases with a genotype collected by MDCH between 2004 and 2012 within 6 months of their diagnosis and exhibiting evidence of TDRM, 76% had resistance to only 1 class of antiretroviral drugs. Among this 76%, PI, NRTI and NNRTI had similar rates of single drug class resistance (21-31%). 24% of the 422 cases had multi-class drug resistance with 4% exhibiting resistance to all three major classes of antiretrovirals used to treat HIV.

Figure 3: TDRM by Drug Class (n=422)



TDRM by Sex, Age, and Race

Figure 4: Percent of Eligible Cases with TDRM, by Sex, Age, and Race

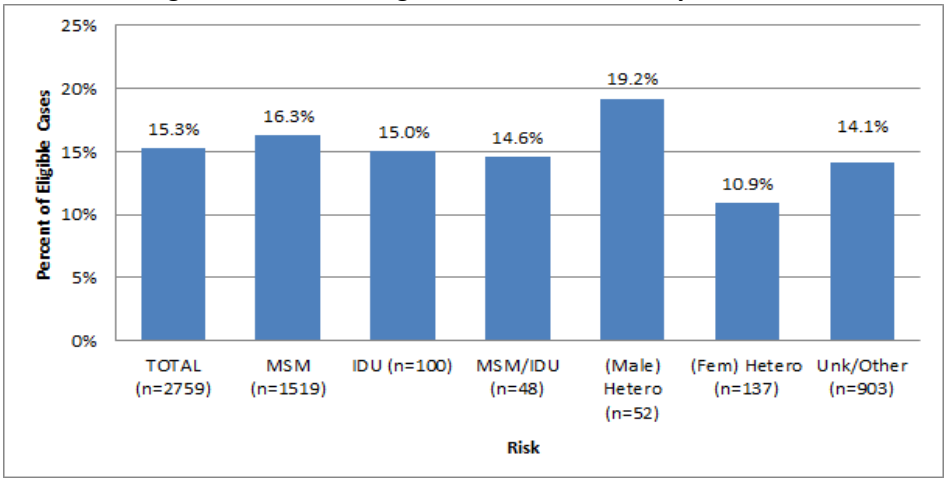


Women have a significantly lower percentage of TDRM compared to the rate overall. The large proportion of TDRM in persons <13 years of age is due to the small number of eligible cases (eight) and is not significant. No age group or race demonstrated a significantly different proportion of TDRM than the total.

TDRM by Risk

Among the new cases with an eligible genotype (n=2,759), males who had heterosexual contact with a high-risk or HIV positive female had the highest rate of TDRM. All other risk categories were comparable to the proportion of TDRM in the total eligible cases.

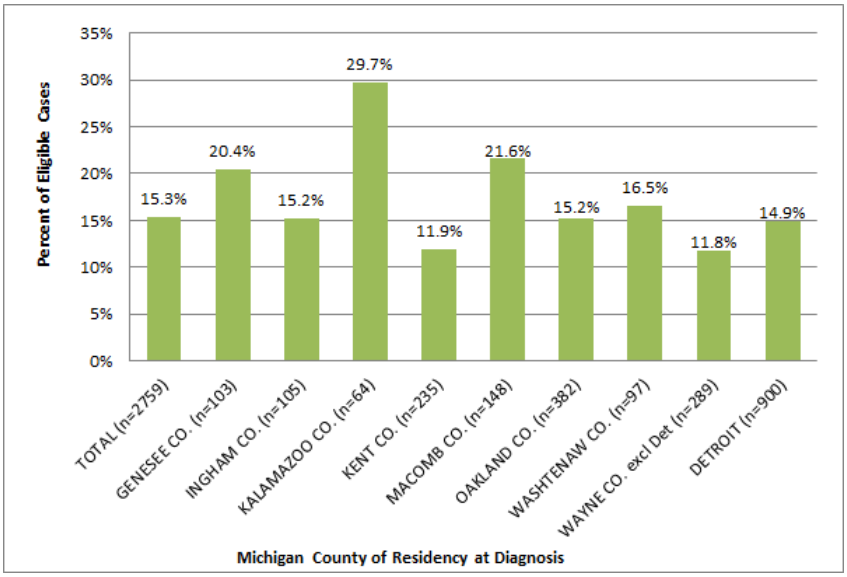
Figure 5: Percent of Eligible Cases with TDRM, by Risk



TDRM by County of Residency at Diagnosis, Top 8 Counties

Eight Michigan counties had over 10 newly diagnosed HIV cases with a genotype collected by MDCH between 2004 and 2012 within 6 months of their diagnosis that exhibited evidence of TDRM. While the city of Detroit had the highest number of cases with TDRM, the percent of cases with TDRM was comparable to the total percent of eligible cases with TDRM in the state overall. The counties with rates of TDRM higher than the state average were: Kalamazoo, Macomb, Genesee, and Washtenaw.

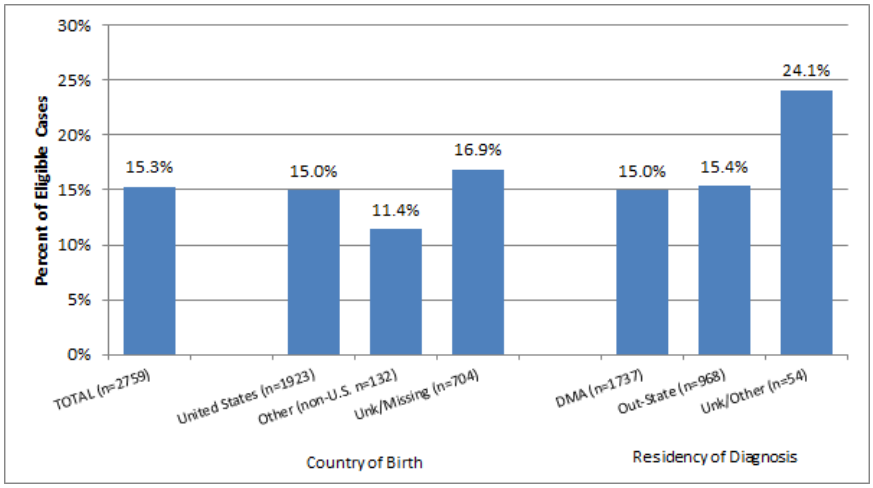
Figure 7: Percent of Eligible Cases with TDRM, by Michigan County of Residence at Diagnosis



TDRM by Country of Birth and Residency at Diagnosis

HIV-positive cases born outside of the U.S. had the lowest rate of TDRM. The 'Unk/Other' category of Residency at Diagnosis had the highest rate of TDRM. This category is the smallest in number and represents those cases diagnosed in other states or countries, as well as those cases of unknown residency.

Figure 6: Percent of Eligible Cases with TDRM, by Country of Birth and Residency at Diagnosis

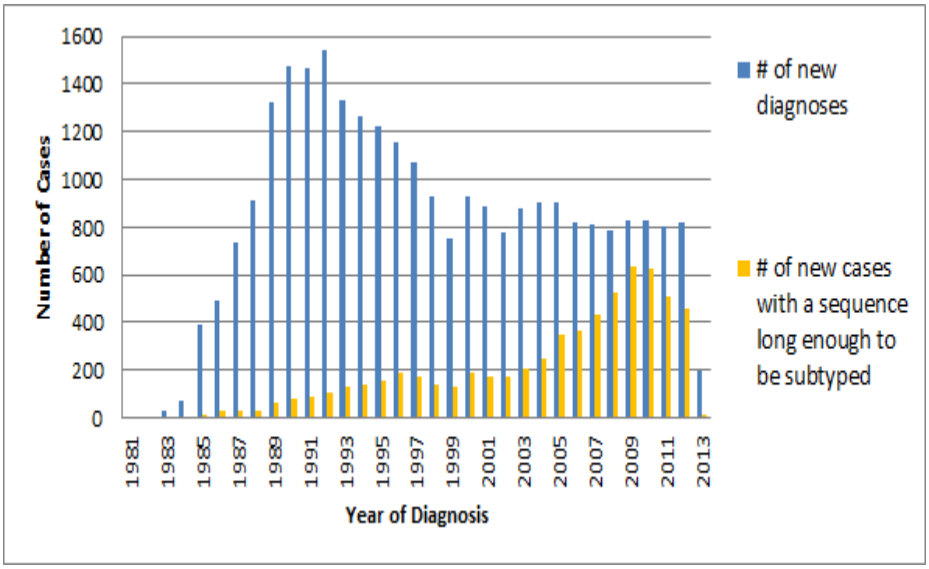


* DMA = Detroit Metropolitan Area and includes Wayne, Oakland and Macomb counties

HIV Subtype or Circulating Recombinant Form

The HIV-1 group M (for Major) virus is the most common form of the HIV virus circulating in the world population. It is estimated that 90% of all infections world-wide are due to HIV-1 group M with an even higher percentage of the infected US population estimated to be group M. HIV-1 group M is further divided into multiple subtypes. Subtype B is the most common form found in Europe, the Americas, Japan, Thailand, and Australia. It is estimated that up to 98% of all HIV infections in the US are HIV-1 group M subtype B. Subtype A is commonly found in West Africa; subtype C is often seen in Southern Africa, India, and Nepal; and subtype D is seen only in Eastern and central Africa[1]. There are also circulating recombinant forms which represent recombination or exchange of genetic material between two HIV subtypes to create a new circulating form of HIV. All 6,137 Michigan cases with a genotype sequence collected by MDCH from 2004-2013 were considered for subtype analysis (Note that this is a slightly different denominator than what has been represented in earlier figures. Because subtype does not change over the course of an individual's infection we did not restrict this investigation to only those genotypes collected within the first 6 months following diagnosis). Figure 8 shows the completeness of genotypes used for subtype analysis by year of diagnosis. Michigan's subtype analysis data spans a wide range of years in which cases were diagnosed, beginning with 1984 and peaking in 2010. This wide range helps to add to the generalizability of the data to all Michigan cases.

Figure 8: Genotype Completeness for Subtype Analysis in Michigan, 1981-2013



*At the time of this analysis, 2013 reporting is not complete.

Figure 9: Subtype category proportions of Cases with a valid genotype in Michigan, diagnosed 1981-2013 (n=6,137)

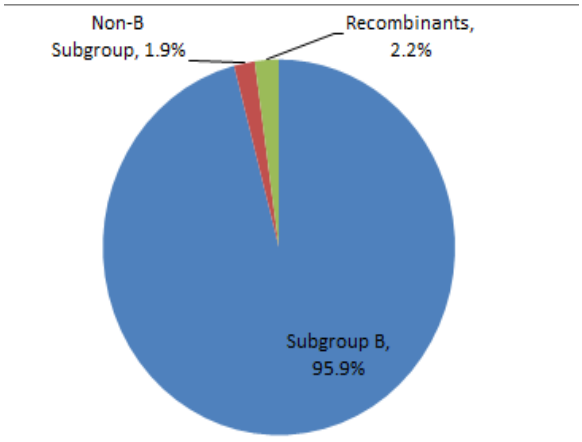


Figure 9 shows the subtype category proportions of all Michigan cases diagnosed 1981-2013 with a genotype sequence collected by MDCH between 2004-2013 (n=6,137). In Michigan, 95.9% of cases were subtype B. This mirrors the national rate of 96.2%. Other subtypes grouped together constituted only an additional 1.9% of the total, leaving 2.2% of Michigan cases with a genotype sequence collected by MDCH between 2004 and 2013 as circulating recombinant forms. Proportions of subtypes among sex, age, race, and risk were all comparable to the total proportion of subtype.

Figure 10 shows the relationship between HIV subtype and country of birth, as well as HIV subtype and residence at diagnosis among genotyped Michigan cases. Note that slightly less than half (48.1%) of cases born outside of the United States are non-B subtype. This is higher than the national average of 29.6% and is indicative of a higher immigration rate of people from areas of the world where non-B subtype HIV is endemic.

Figure 10: Percent of Subtypes by Country of Birth, and Residence at Diagnosis (n=6,137)

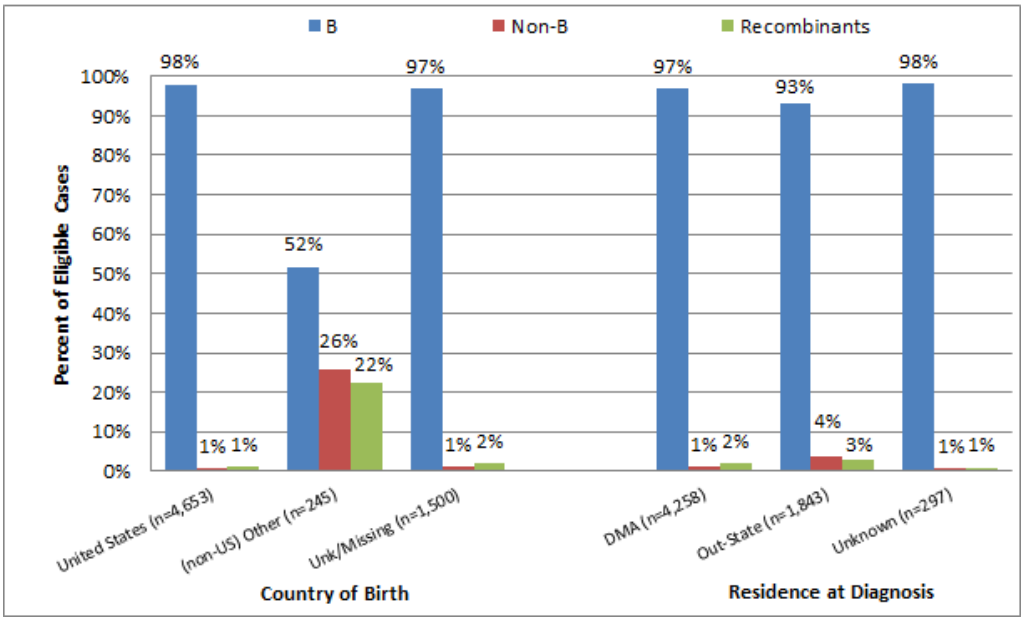
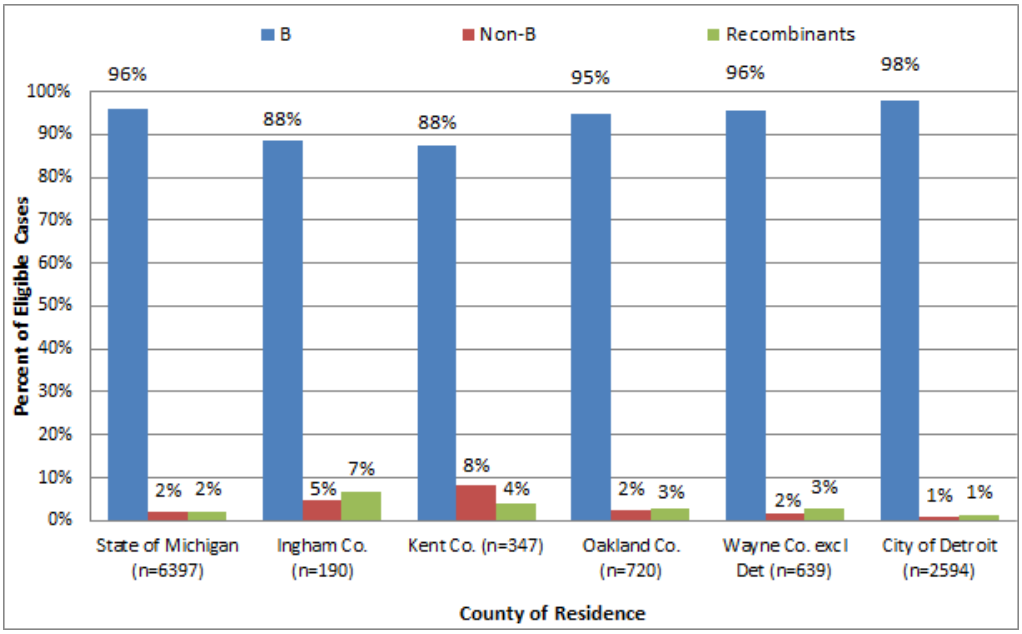


Figure 11: Percent of Cases by Subtype and County of Residence at Diagnosis (n=6,137)



The four Michigan counties with the largest *counts* of non-B HIV cases among genotyped Michigan cases were Ingham, Oakland, Kent and Wayne Counties. Figure 11 shows the percent of persons diagnosed with non-B HIV in each county and the city of Detroit. The data show that Ingham, Kent, and Oakland counties are the only counties that have rates of non-B HIV higher than the overall state rate. Given that the primary origin of non-B HIV is African countries, these unusually high rates of non-B HIV are explained by the high proportion of African-born persons living in Ingham and Kent counties at the time of their diagnosis. Of all foreign-born persons living with HIV in Michigan as of 2012, 5% lived in Ingham county and 22% lived in Kent county . Of these persons, 58% and 49% in Ingham and Kent counties respectively were African in origin—higher than the 41% of foreign-born persons living with HIV statewide who immigrated from Africa.